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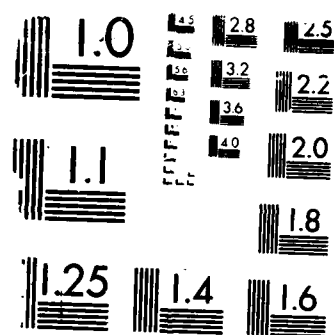
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This work has defined the effects of exercise, of exercise in hypoxia and of sleep in hypoxia on lung and chest wall function. We determined the causes of periodic breathing during sleep in hypoxia, showed who might be susceptible to periodic breathing and demonstrated the effects of acclimatization. We also showed that respiratory muscle fatigue might be an important determinant of endurance performance in the highly fit.

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FINAL SCIENTIFIC REPORT
(February 1, 1977 to February 1, 1986)

Jerome A. Dempsey, Ph.D.

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We have completed work concerned with 6 major problems related to performance of the pulmonary system during exercise and sleep in hypoxia.

1. Endurance Exercise Performance

The question of respiratory muscle fatigue during exercise in humans was studied in highly fit subjects performing high intensity exercise to exhaustion. First we found that a partial "unloading" of ventilatory work--by breathing low density He:O₂ gas mixtures--significantly increased exercise endurance time to exhaustion and reduced "perception" of effort. On the other hand our additional data did not implicate the mechanical work of breathing during exhaustive exercise as an important contribution to overall fatigue. We determined the pleural pressure wave form and magnitude generated each breath during exhaustive exercise. Then we mimicked this form and magnitude of pressure development at rest and found that the subject could tolerate this form of pressure development for much longer times than he could exercise. Work continues on this project in normoxic and hypoxic conditions with the added aim of determining the oxygen cost of breathing.

2. Regulation of Breathing

We have studied respiratory muscle recruitment during exercise and saw evidence of active expiration even in mild exercise. We documented this by measuring the change in functional residual capacity and in end-expiratory volume and in esophageal and gastric pressures. We also verified these changes by recording augmented abdominal muscle EMG activity even at light work loads.

3. Work of Breathing in Exercise

We showed both advantages and disadvantages to active expiration during exercise. On the one hand, this causes the inspiratory muscles to be lengthened so they can develop more tension (on the subsequent inspiration following active expiration) and may even spare diaphragmatic contraction at the initiation of inspiration. On the other hand, the fall in FRC reduces lung compliance and therefore increases the elastic work of breathing. We believe the net effect is a beneficial one.

4. Voluntary vs. Involuntary Control of Breathing

Popular opinion suggests that voluntarily controlling our breathing pattern may be beneficial to gas exchange--especially under stressful conditions such as exercise in hypoxia. We compared the mechanical work of breathing between maximum exercise and when that identical breathing pattern was voluntarily mimicked--using visual feedback--at rest. As intended, the involuntary and the voluntary controlled breathing patterns were identical in terms of flow rate and tidal volume, and end-expiratory lung volume--even the relative contributions of rib cage and abdomen were similar in the two conditions. However, the pleural pressure exerted during expiration was 1.5 to 2.5 times greater during voluntary (vs. spontaneous) breathing. Thus during voluntary control apparently the feedback of excessive pressure developed by the respiratory muscles was ignored or overridden by cortical influences--the result is substantially wasted effort by the respiratory muscles to produce the same flow. Clearly these results support the concept that the normal control system is best left to its own "natural" feedback devices--even under the extreme demands of maximum exercise.

Finally, we have presented the concept in two recent reviews and presentations (Am. J. Cardiology, 1985; and Wolffe Memorial Lecture, American College of Sports Medicine, May 1985) that the lung becomes a "limiting" factor to exercise capacity as one proceeds from an untrained state to a highly trained state, because training causes adaptation of the locomotor muscles but not the respiratory muscles nor the lung. Eventually the capability for O_2 uptake by the locomotor muscles becomes greater than that afforded by the O_2 transport capabilities of the lung and chest wall. This selective effect of physical training contrasts markedly with that of the long-term resident of high altitude who shows true structural adaptations of the pulmonary system.

5. Individual Susceptibility to Exercise-Induced Hypoxemia in a Hypoxic Environment

We studied fit, healthy subjects during very heavy exercise and determined the relative contribution of various factors which would cause marked hypoxemia when very mild levels of hypoxia were imposed (.17 to .18 inspired % O_2) on 4 to 6 runs of exercise at 85 to 95% of max VO_2 . Two factors clearly dominated the cause of marked hypoxemia under these conditions:

- 1) The absolute exercise oxygen consumption. The fitter the subject, the higher the VO_2 --thus the lower the mixed venous O_2 content and the greater the probability for incomplete gas exchange. Arterial PO_2 was fairly well maintained in normal subjects at resting levels (PaO_2 75-80 mmHg)--whereas, in the highly fit PaO_2 fell 20 to 30 mmHg during exercise.
- 2) The magnitude of the ventilatory response. The subject whose ventilation responded vigorously to the combination of exercise plus

hypoxia tended to defend his resting PaO_2 better than the subject--even the highly fit subject--who did not ventilate vigorously. Of course the physiologic cost of this extra ventilation may present yet another problem to the performance of the endurance athlete at high altitude. (See Aim 1 above.)

6. Sleep in Hypoxia

We completed our study of the relationship between hypoxia-induced periodic breathing in sleep and the occurrence of obstructive apnea. We used normal subjects and those who might be "susceptible" to upper airway closure, i.e., heavy snorers and even some patients with obstructive sleep apnea syndrome. As expected we found that administration of hypoxia caused immediate hypocapnia leading to a Cheyne-Stokes type of oscillatory breathing pattern which caused marked increases in airway resistance during the periods of low ventilatory drive. The surprising finding was that once full-blown periodic breathing developed--after about 5 minutes of hypoxia--airway resistance was markedly reduced to levels \leq than those observed while awake and no evidence of occlusive apnea occurred. The conclusion is that hypoxia must have exerted a protective effect on the upper airway, by ensuring that as inspiratory drive increased toward the end of each apneic period, activity to the muscles controlling upper airway caliber was greater than and/or preceded that to the diaphragm and other inspiratory muscles of the chest wall. Further studies are now needed of the EMG activity of these upper airway and chest wall muscles to determine their relative activities during the apneic periods. This "protective" mechanism is central to the sojourner at high altitude--particularly the heavy snorer--to guard against occlusive apnea and even greater nocturnal hypoxemia.

Military Significance

Our contract work is aimed at a better understanding of two physiological problems occurring in hypoxic environments which clearly affect the well-being and performance capabilities of the human sojourner at high altitudes. These problems are periodic breathing during sleep leading to loss of quality sleep and the resulting daytime hypersomnolence and fatigue; and the regulation of the ventilatory response and pulmonary gas exchange during exercise in hypoxia which are key determinants of exercise performance.

Our work on periodic breathing during hypoxic sleep provides the first comprehensive, quantitative description of this problem and provides the first definitive evidence detailing the major causes of periodicity and the reasons behind the beneficial effects of acute O_2 administration. Further, our more recent data suggests that acclimatization over a matter of a few days at high altitude may greatly alleviate periodic breathing during sleep. However, this remains a highly individual characteristic which we were unable to predict from available measurements. Indeed, the test of acute hypoxic ventilatory response--which is commonly used as a predictor of many facets of acclimatization--had no predictive value at all for the occurrence or severity of periodic breathing in hypoxic sleep.

Exercise capacity as determined by the pulmonary system in hypoxia and the debilitating symptoms of dyspnea which accompany exercise in hypoxia have been the subject of our investigations. Our work has detailed the critical limitations to oxygen transport presented by the failure of the lung's gas exchange and ventilatory control system and chest wall mechanics to respond adequately and/or efficiently to heavy work in hypoxic environments. Further, the baseline work in normoxic environments clearly shows the susceptibility of some highly fit individuals to these problems during exercise, thereby providing a basis for prediction of problems with high altitude exercise from measurements made at sea-level. We also showed the simple use of exercise tests in acute hypoxia--even using non-invasive measurements of arterial O_2 saturation--should provide excellent prediction of gas exchange "failure" at high altitudes. Our recent findings also strongly implicate a highly significant role for pulmonary and chest wall mechanics in the regulation of ventilation--and thus of gas exchange--during exercise--especially hypoxic exercise. We would predict with some confidence that the sea-level native with even "mild." asymptomatic airway disease (such as that due to chronic cigarette smoking or the mostly reversible airway disease of the otherwise healthy asthmatic) will have substantial problems in maintaining arterial oxygenation and/or avoiding extreme dyspnea during exercise at even mild elevations in altitude.

PUBLICATIONS

Manuscripts Published or In Press

1. Berssenbrugge, A., J. Dempsey, C. Iber, J. Skatrud, and P. Wilson. Mechanisms of hypoxia-induced periodic breathing during sleep in humans. J. Physiol. (London) 343:507-524, 1983.
2. Berssenbrugge, A., J. Dempsey, and J. Skatrud. Hypoxic versus hypocapnic effects on periodic breathing during sleep. In: High Altitude and Man, American Physiological Society, pg. 115-127, 1984.
3. Berssenbrugge, A., J. Dempsey, and J. Skatrud. Effects of sleep state on ventilatory acclimatization to hypoxia in humans. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 57:1089-1096, 1984.
4. Dempsey, J.A. Ventilatory control during sleep in hypoxia: Overview. In: Progress in Clinical and Biological Research, Hypoxia Symposium III, Banff, Canada, January 1983, J. Sutton and C. Houston (eds). Vol. 136, pg. 61-64, 1984.
5. Dempsey, J.A., P.G. Hanson, and K. Henderson. Exercise-induced arterial hypoxaemia in healthy humans at sea level. J. Physiol. (London) 355:161-175, 1984.
6. Fregosi, R. and J. Dempsey. Regulation of arterial acid-base status in the exercising rat. J. Appl. Physiol. 57:396-402, 1984.
7. Wilson, P., J.B. Skatrud, and J.A. Dempsey. Effects of slow-wave sleep on ventilatory compensation to inspiratory elastic loading in humans. Respir. Physiol. 55:103-120, 1984.
8. Dempsey, J.A., E.H. Vidruk, and G.S. Mitchell. Regulation of pulmonary control systems during exercise: Update. Fed. Proc. 44:2260-2270, 1985.
9. Dempsey, J. and R. Fregosi. Adaptability of the pulmonary system to changing metabolic requirements. Am. J. Cardiology 55(10):59D-67D, April 1985.
10. Hussain, S.N.A., R.L. Pardy, and J. Dempsey. Mechanical impedance as a determinant of inspiratory neural drive during exercise in healthy humans. J. Appl. Physiol. 59(2):365-375, 1985.
11. Skatrud, J.B. and J.A. Dempsey. Airway resistance and respiratory muscle function in snorers during NREM sleep. J. Appl. Physiol. 59(2):328-335, 1985.
12. Dempsey, J., J. Skatrud, and A. Berssenbrugge. Sleep and breathing in hypoxia. In: Contemporary Issues in Pulmonary Disease, N. Edelman and T.V. Santiago (eds). Churchill Livingstone, London, Vol. 5, pg. 81-114, 1986.

13. Fregosi, R. and J.A. Dempsey. The effects of exercise in normoxia and acute hypoxia on respiratory muscle metabolites. J. Appl. Physiol. 60:1274-1283, 1986.
14. Fregosi, R., and J.A. Dempsey. Anesthetic effects on $[H^+]_a$ and muscle metabolites at rest and following exercise. Resp. Physiol. 65:85-98, 1986.
15. Smith, C.A., and J.A. Dempsey. Carotid bodies are required for ventilatory acclimatization to chronic hypoxia. J. Appl. Physiol. 60:1003-1010, 1986.
16. Dempsey, J.A., and J. Skatrud. A sleep-induced apneic threshold and its consequences. Am. Rev. Resp. Dis. 133:1163-1170, 1986.
17. Dempsey, J.A. Is the lung built for exercise? J.B. Wolffe Memorial Lecture, Medicine and Science in Sports and Exercise 18(2):143-155, 1986.
18. Begle, R.L., J.B. Skatrud, and J.A. Dempsey. Ventilatory compensation for changes in functional residual capacity during sleep. (In press).

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